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WHATIS CLAIMED IS:

- 1. A portable DNA sequence comprising a series of nucleotides capable of directing intrace/lular production of metalloproteinase inhibitors.
- 2. The portable DNA sequence of claim 1 wherein said sequence is capable of directing intracellular production of collagenase inhibitors.
- 3. The portable DNA sequence of claim 1 wherein said nucleotide sequence is:

:					
10 GTTGTTGCTG	20 TGGCTGATAG	CCCCAGCAGG	40 GCCTGCACCT	50 GTGTCCCACC	CCACCCACAC
70 ACGGCCTTCT	80 GCAATTCCGA	90 CCTCGTCATC	100 AGGGCCAAGT	110 TCGTGGGGAC	120 ACCAGAAGTO
130 AACCAGACCA	140 CCTTATACCA	J50 GCGTTATGAG	160 ATCAAGATGA	170 CCAAGATGTA	180 TAAAGGGTTO
190 CAAGCCTTAG	200 GGGATGCCGC	210 TGACATCCGG	220 TTCGTCTACA	230 CCCCCGCCAT	24(GGAGAGTGT(
250 TGCGGATACT	260 TCCACAGGTC	270 CCACAACCGC	280 AGCGAGGAGT	290 TTCTCATTGC	30(TGGAAAACT(
310	320 TCTTGCACAT	330	340	350	360
370	/	390	400	410	42(
430	440 TATCCATCCC	450	460	470	48
. 490	/	510	520	530	54
550/	/	570	580	590	60·

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610 620 630 640 650 660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGACA
670 680 690 700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC

- 4. The portable DNA sequence of claim 2 wherein said sequence is capable of directing intracellular production of a collagenase inhibitor biologically equivalent to that isolable from human skin fibroblasts.
- 5. A recombinant-DNA cloning vector comprising a nucleotide sequence capable of directing intracellular production of metalloproteinanse inhibitors.
- 6. The vector of claim 5 wherein said vector comprises a nucleotide sequence containing at least the following nucleotides:

20 30 GTTGTTGCTG TGGCTGATAG /CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG 90 100 ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC AACCAGACCA CCTTATACCA GGGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC 130 40 160 180 190 200 210 220 230 CAAGCCTTAG GGGAT/GCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC 280 TGCGGATACT TCCÁCAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAAACTG 310 320 330 340 350 360 CAGGATGGAC TØTTGCACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC 370 380 390 400 410 TTAGCTCAGC /GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG 440 450 460 TTTCCCTGT/T TATCCATCCC CTGCAAACTG; CAGAGTGGCA CTCATTGCTT GTGGACGGAC

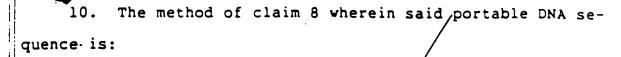
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CAGCTCTCC AAGGCTCTGA AAAGGGCTTC/CAGTCCCGTC ACCTTGCCTG CCTGCCTCGC 5/10 GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCGG GTGGAAGCTG AAGCCTGCAC AGT/STCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGAC *(19*90 ATGAAATAAA GAGTTACCAC QCAGCAAAAA AAAAAAGGAA TTC The vector puc9-F5/237P10.

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- 8. A recombinant-DNA method for microbial production of a metalloproteinase inhibitor comprising:
 - (a) preparation of a portable DNA sequence capable of directing a host microorganism to produce a protein having metalloproteinase inhibitor activity;
 - (b) cloning the portable DNA sequence into a vector capabl of being transferred into and replicating in a host mi croorganism, such vector containing operational elements for the portable DNA sequence;
 - (c) transferring the vector containing the portable DNA se quence and operational elements into a host microorganism capable of expressing the metalloproteinase inhib itor protein;
 - (d) culturing the host microorganism under conditions appropriate for amplification of the vector and expression of the inhibitor; and
 - (e) in either order:
 - (i) harvesting the inhibitor; and
 - (ii) the inhibitor to assume an active, tertiary structure whereby it possesses metalloproteinase inhibitor activity.
- 9. The method of claim 8 wherein said metalloproteinase inhibitor is collagenase inhibitor.

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			/		
10 GTTGTTGCTG	20 TGGCTGATAG	30 CCCCAGCAGG	GCCTGCACCT	50 GTGTCCCACC	60 CCACCCACAG
70 ACGGCCTTCT	80 GCAATTCCGA	90 CCTCGTCATC	100 AGGGCCAAGT	110 TCGTGGGGAC	120 ACCAGAAGTC
130 AACCAGACCA	140 CCTTATACCA	150 GCGTTATGAG	160 ATCAAGATGA	170 CCAAGATGTA	180 TAAAGGGTTC
	200 GGGATGCCGC	210/ TGACATCCGG	220 TTCGTCTACA	230 CCCCCGCCAT	240 GGAGAGTGTC
250 TGCGGATACT	260 TCCACAGGTC	270 CCACAA¢CGC	280 AGCGAGGAGT	290 TTCTCATTGC	300 TGGAAAACTG
	320 TCTTGCACAT				
	380 GCCGGGGCTT				
	440 TATCCATCCC				
	500 AAGGCTCTGA				540 CCTGCCTCGG
550 GAGCCAGGGC	TGTGCACCTG		CGGTCCCAGA	TAGCCTGAAT	CCTGCCCGGA
610 GTGGAAGCTG	620 AAGGCTGCAC	630 AGTGTCCACC			
670 ATGAAATAAA	680 GAGTTACCAC			TTC	

- The method of claim 8 wherein said vector containing said portable DNA sequence is pUC9-F5/237P10.
- The method of claim 8 wherein said host microorganism is a bacterium.

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- 13. The method of claim 12 wherein said bacterium is a member of the genus <u>Bacillus</u>.
- 14. The method of claim 13 wherein said bacterium is Bacillus subtilis.
- 15. The method of claim 12 wherein said bacterium is Escherichia coli.
- 16. The method of claim 12 wherein said bacterium is a member of the genus <u>Pseudomonas</u>.
- 17. The method of claim 16 wherein said bacterium is Pseudomonas aeruginosa.
- 18. The method of claim 8 wherein said host microorganism is a yeast.
- 19. The method of claim 8 wherein said yeast is Saccharomyces cerevisiae.
- 20. The method of claim 8 wherein said inhibitor is harvested prior to being caused to assume said active, tertiary structure.
- 21. The method of claim 8 wherein said inhibitor is caused to assume said active, tertiary structure prior to being harvested.
- 22. A metalloproteinase inhibitor which is biologically equivalent to the collagenase inhibitor isolable from human skin fibroblasts produced by the method of claim 8.

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ADD (23)

- 23. The microorganism C600/pUC9-F5/23/P10 having ATCC Accession No. 53003.
- 24. The portable DNA sequenc of claim 1 wherein said nucleotide sequence is:

, nacreotiat	e sequence i	S:			
	20 GCAGATCCAG				
GACCCCTGGC	80 TTCTGCATCC	90 TGTTGTTGCT	100 GTGGCTGATA) 110 GCCCCAGCAG	12 GGCCTGCAC
TGTGTCCCAC	140 CCCACCCACA	150 GACGGCCTTC	160 TGCAATTCCG	170 ACCTCGTCAT	18 CAGGGCCAA
	200 CACCAGAAGT				
cc.a.a.i.d.	260 ATAAAGGGTT	CCAAGCCTTA	GGGGATGCCG	CTGACATCCG	GTTCGTCTA(
	TGGAGAGTGT	YTGCGGATAC	TTCCACAGGT		CAGCGAGGA(
TTTCTCATTG	CIGGAAAACI	GCAGGATGGA	CTCTTGCACA		CAGTTTCGTC
GCTCCCTGGA	440 ACAGCCTGAG	CTTAGCTCAG	CGCCGGGGCT	TCACCAAGAC	CTACACTGTT
	AATGCACAGT				
ACTCATTGCT	TGT GACGGA	CCAGCTCCTC	CAAGGCTCTG	AAAAGGGCTT	CCAGTCCCGT
610 CACCTTGCCT	GCTGCCTCG				
ATAGCCTGAA	TCCTGCCCGG	690 AGTGGAAGCT	700 GAAGCCTGCA	710 CAGTGTCCAC	720 CCTGTTCCCA
730 CTCCCATCT/T	740 TCTTCCGGAC	750 AATGAAATAA	760 AGAGTTACCA	770 CCCAGCAAAA	780 AAAAAAAGGA

add B22

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